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심외막지방 측정을 통한 복부 내장 지방과 골무기질량의 연관성 분석

Association of visceral fat via epicardial fat thickness with bone mineral content in Korean Healthy Twin Study

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<Abstract>

Association of visceral fat via epicardial fat thickness with bone mineral content in Korean Healthy Twin Study

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Despite the detrimental effects of abdominal visceral fat on many cardiovascular and metabolic diseases, the relationship between abdominal visceral obesity and osteoporosis remains controversial. In the present study, we investigated the association between bone mass and abdominal fat estimated by echocardiographic epicardial fat thickness, which is a surrogate measure of abdominal visceral fat, anthropometric data, and regional fat mass (FM) measured by dual energy x-ray absorptiometry (DXA). A total of 1198 subjects (525 men, 460 premenopausal women, and 213 postmenopausal women) were selected from the Healthy Twin Study,

a nationwide Korean twin and family study. Epicardial fat thickness was measured on the free wall of the right ventricle at end-systole from the parasternal long axis views. Total FM, regional FM, lean mass (LM), and bone mineral content (BMC) were measured by DXA. We performed multiple linear regression analysis with two models to determine the association between abdominal visceral obesity and osteoporosis. Age and height were included as covariates in Model 1. Past medical history and behavioral factors were included in Model 2. Epicardial fat thickness was positively associated with BMC in all three subgroups (men, premenopausal women, and postmenopausal women) in Model 1 and in Model 2. Trunk FM, waist circumference, and waist-to-hip ratio were also positively correlated to BMC in all three subgroups. Together, these findings suggest that abdominal visceral fat has a positive effect on BMC in the Korean population.

Key words: visceral fat, bone mineral content, epicardial fat, obesity, osteoporosis

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I. Introduction

Obesity and osteoporosis are significant public health problems with increasing prevalences and substantial economic burdens in most industrialized countries. In the United States of America (USA), in 2010, more than 10 million older adults had osteoporosis and the annual direct medical costs related to osteoporosis were estimated to be $17 to $20 billion.[1,2] In the same year, more than 35% of adults were obese. The total economic burden of obesity in the USA is estimated to increase by $50 to $60 billion per year by 2030.[3,4] The prevalences of obesity and osteoporosis in Korea are similar: approximately 30% of adults are classified as obese and 13.1% of men and 24.3% of women aged 40 to 79 years old are estimated to have osteoporosis.[5,6]

Obesity has a negative effect on most health conditions, especially cardiovascular and metabolic diseases, but obesity has been shown to reduce osteoporosis. Previous epidemiological studies have demonstrated a positive relationship between obesity parameters and bone mineral density (BMD).[7-10] Several underlying mechanisms support this hypothesis: (1) the bone remodeling process is adaptive to increased weight bearing,[11-

[13] (2) osteoclasts are suppressed by the adipocytes that produce estrogen,[14,15] and (3) osteoblasts are activated by increased anabolic hormones such as insulin and insulin-like growth factor-I, which are related to obesity.[16-18] However, obesity has not been conclusively determined to have a positive effect on osteoporosis. Most previous studies used anthropometric data such as body mass index (BMI) and waist circumference (WC) to assess obesity and these factors did not accurately reflect the quantity of fat. Also, recent data have demonstrated that different regional fats have different functions. Therefore, the exact relationship between fat and osteoporosis needs to be investigated.[19-21]

Visceral obesity may offer new insight into the relationship between fat and osteoporosis due to its unique association with inflammation, which is also closely involved with bone metabolism.[22-24] Recently, several reports have indicated that visceral obesity has a negative effect on bone mass,[25,26] but this association is controversial due to the difficulty in measuring visceral fat. The gold standard methods of measuring visceral fat are direct measures of fat volume using computed tomography (CT) or magnetic resonance imaging (MRI). However, these techniques have several

limitations including exposure to hazardous radiation and high costs. Dual energy x-ray absorptiometry (DXA) is widely used for measuring abdominal fat mass (FM) due to its relatively low cost and minimal radiation exposure, but it cannot distinguish visceral fat from abdominal subcutaneous fat. As stated, anthropometric measures such as WC and waist-to-hip ratio do not accurately measure fat quantity.

In this study, we introduce epicardial fat thickness as a surrogate marker of visceral fat. We used this measurement, as well as anthropometric data and regional FM measured by DXA, to investigate the association between visceral obesity and bone mass. Epicardial fat located between the myocardium and the visceral pericardium has the same embryologic origin as intra-abdominal visceral fat. The use of transthoracic echocardiography to measure epicardial fat thickness is a simple and reliable imaging method for predicting visceral fat.[27]

II. Methods

Study design and population

The subjects included in this analysis were participants in the Healthy Twin Study, which was a nationwide population-based cohort study implemented as part of the Korean genome epidemiology study. It was initiated in 2005 and participants continue to receive follow-up examinations every 3 years. Participants consisted of a twin pair and their first degree family members. All participants received medical examinations and completed detailed questionnaires about life style and epidemiologic information at one of three medical school-affiliated hospitals. Details on the study design and protocols have been published previously.[28]

Among the initial 1467 subjects who completed an echocardiogram and body composition measurements between 2006 and 2008, 269 subjects were excluded: 220 subjects were excluded for poor echocardiographic image quality such as poor echo window or angle difference and 49 subjects were excluded for a treatment history of osteoporosis. A total of 1198 subjects (525 men, 460 premenopausal women, and 213 postmenopausal women) were included in our final

analysis. Women were considered to be postmenopausal if they had no history of menstruation during the previous year and fulfilled at least one of the following conditions: natural menopause, use of estrogen replacement therapy, or age older than 55 years. All participants provided written informed consent. The study protocol was approved by the Institutional Review Board at Seoul National University School of Public Health.

Measurement of epicardial fat thickness

Subjects underwent transthoracic echocardiogram according to standard techniques in the left lateral decubitus position using commercially available instruments (GE, USA). The images were recorded onto a digital database. The measurement of epicardial fat thickness was performed by two cardiologists using an offline DICOM (Digital imaging and Communications in Medicine) viewer (Onis 2.5 professional version). The cardiologists were unaware of the subjects' clinical information.

Epicardial fat thickness was identified as the echo-free space between the myocardium and the visceral epicardium, and its thickness was measured perpendicularly on the free wall of the right ventricle at end-

systole from the standard parasternal long axis view.[29] To standardize the measurements between observers, the aortic annulus was used as an anatomical landmark and the epicardial fat thickness was measured at the point on the free wall of the right ventricle along the midline of the ultrasound beam, perpendicular to the aortic annulus (Figure 1).[30] The intra- and inter-observer agreement for the measurement of epicardial fat thickness were good and the intra-class correlation coefficients were 0.95 (range, 0.93-0.97) and 0.92 (range, 0.88-0.95), respectively (Figure 2).

Measurement of anthropometric data and body composition

Body weight and height were measured according to standard methods while the subjects were wearing a light gown or light indoor clothing. Minimum WC was measured in the standing position at the point between the lower rib margin and the iliac crest. Hip circumference was measured as the largest circumference over the buttock. BMI was calculated as weight divided by height squared (kg/m2) and the waist-to-hip ratio was calculated as WC divided by hip circumference. Total bone

mineral content (BMC), bone mineral density (BMD) of the whole body, the lumbar spine, and the pelvis, whole-body and regional FM, and lean mass (LM) were measured using DXA (Delphi W, Hologic, Boston, MA, USA). Skeletal muscle mass (SM) was measured using a bioelectrical impedance analysis (BIA) meter (Biospace, Inbody720, Korea). The DXA and BIA equipment were calibrated by the manufacturer. The coefficients of variation for BMC, BMD, FM, LM, and SM measurements were < 1%. Percent FM was calculated as FM/(FM + LM + BMC) × 100.

Clinical information

The following clinical and demographic data were extracted from each patient's baseline questionnaire: past medical history of chronic diseases including hypertension, diabetes mellitus, thyroid disease, and osteoporosis; female reproductive history including age at menopause and use of estrogen replacement therapy; and information about cigarette smoking, alcohol consumption and exercise habits.

Statistical analysis

The value of each continuous variable is expressed as a mean ± standard deviation. Each categorical or discrete variable is presented as a percentage. Comparisons among the groups (men, premenopausal women, and postmenopausal women) were performed using analysis of variance (ANOVA), analysis of covariance (ANCOVA), and the chi squared (χ^2) test. Multiple comparisons between two groups were performed with post hoc analysis. The relationships between the epicardial fat thickness and other measures of body composition were analyzed with Pearson's correlation analysis. Two multiple linear regression models in each group were used to evaluate associations between visceral obesity and bone mass; age and height were included as covariates in regression Model 1 and past medical history (hypertension, diabetes mellitus, and thyroid disease), and smoking, alcohol, and exercise habits were added as covariates in Model 2. We also evaluated associations between BMC and body composition variables using a linear mixed model to correct for familiar interdependence. Age, height, hypertension, diabetes, hyperthyroid disease, smoking habits, alcohol consumption, and regular exercise were adjusted as fixed effects,

and family unit was adjusted as a random effect. Statistical analyses were performed using SPSS 18.0 for Windows (Chicago, IL, USA). All tests were two-tailed, and a *p*-value < 0.05 was considered statistically significant.

III. Results

The baseline characteristics of the subjects are listed in Table 1. The body composition parameters and clinical information are statistically different according to gender and menopausal status. Men had higher BMI, WC, waist-to-hip ratio, LM, and SM than women. Fat-related parameters such as FM and trunk FM were lower in men than in women, with the exception of head FM. Postmenopausal women had more total fat and trunk fat, but had lower leg fat, LM, and SM than premenopausal women. Epicardial fat thickness was highest in postmenopausal women and lowest in premenopausal women. BMC was higher in men due to their larger body size compared with women. However, the difference in BMD between the genders was small and no significant difference in spine BMD was identified between men and premenopausal women. Hypertension and diabetes mellitus were most prevalent in postmenopausal women; risky heath behaviors such as smoking and drinking alcohol were highest in men.

Figure 3 and Table 2 show the correlations of epicardial fat thickness with anthropometric and body composition variables. Epicardial fat thickness was highly associated with body FM, especially trunk FM in

postmenopausal women. Epicardial fat thickness was also associated with classical central obesity parameters such as WC and waist-to-hip ratio. Epicardial fat was positively correlated with age, but BMC was negatively correlated with age. BMC showed a strong positive correlation with height.

We also examined the difference in whole-body BMC, whole-body BMD, and body-part specific BMD across the tertiles of epicardial fat thickness, adjusting for age and height in all three subgroups using the ANCOVA test. As shown in Table 3, BMC significantly increased across increasing tertiles of epicardial fat thickness in all subgroups. This tendency was not observed in whole-body or spine BMD, particularly in women.

Figure 4 shows the association between BMC and epicardial fat thickness and trunk fat. In bivariate unadjusted analyses, BMC increased with increasing epicardial fat thickness in all subgroups. These tendencies were also observed in associations between BMC and trunk fat in the subgroups.

Table 4 shows the multivariable adjusted associations between BMC and body composition variables. Epicardial fat thickness was

positively associated with BMC in men, premenopausal women, and postmenopausal women in the age- and height-adjusted model (Model 1). The association was unchanged after controlling for past medical history (hypertension, diabetes, and hyperthyroid disease) and behavioral factors (smoking, alcohol, and exercise habits; Model 2). Trunk FM and classical indices of abdominal obesity parameters such as WC and waist-to-hip ratio were also positively associated with BMC in both models. The same associations were observed with total FM. After correcting for familial interdependence using a linear mixed model, the association between abdominal fat and BMC was still positive (Table 5).

Approximately 15% of the initial subjects were excluded from analysis due to poor echocardiographic images that affected measurement reliability (Supplemental Figure 1). These subjects were younger and had lower total fat and abdominal fat, including epicardial fat thickness, than the subjects with good echocardiographic images (Supplemental Table 1). The associations between BMC and abdominal fat did not change when subjects with poor echocardiographic images were included in the analysis. The β coefficient of the association between epicardial fat and BMC in

Model 2 was 0.117 for men (SE: ± 0.020, *p*-value = 0.000), 0.076 for premenopausal women (SE: ± 0.020, *p*-value = 0.000), and 0.065 for postmenopausal women (SE: ± 0.022, *p*-value = 0.003).

IV. Discussion

The results from our study of the Korean Healthy Twin cohort showed that visceral fat estimated from epicardial fat thickness was positively associated with BMC regardless of gender and menopausal status. Its relationship was also evident with other abdominal obesity parameters such as WC, waist-to-hip ratio, and trunk fat.

The exact association between fat and bone is still controversial, but this relationship has long been an interesting research topic among epidemiologists. Several previous studies reported positive associations between fat and BMC or BMD and two plausible mechanisms have been suggested on the basis of two main characteristics of fat.[31] One mechanism is related to increased weight bearing of bones, which directly activates adaptive bone remodeling; [11-13] the other mechanism is associated with paracrine and hormonal effects of fat, which enhance anabolic effects on bone through increased production of sex hormones and hormonal factors such as insulin, leptin, and amylin.[14-18] However, other previous reports demonstrated a negative relationship between fat and BMC or BMD.[9,32-34] In most of these studies, body weight was used as an important covariate

in the analysis, but this may cause a false association between FM and bone mass due to biases from strong co-linearity between FM and body weight.[35] On the basis of this methodology, we did not use body weight as a covariate for investigating influences of fat on bone mass and BMD. Instead of weight, we used height as an important covariate because whole-body BMC and BMD are highly associated with whole-body bone size, and height is known to be a good surrogate marker for body and bone size .[31,32]

Abdominal visceral fat has unique characteristics compared with other fat such as subcutaneous fat.[26,36] Therefore, a simple and accurate method for measuring abdominal visceral fat is necessary to investigate the exact association between abdominal visceral fat and bone mass. Although CT and MRI are gold standard methods of measuring visceral fat, they present challenges for use in a large study due to exposure to hazardous radiation and high costs. Therefore, DXA is the most widely used technique for measuring abdominal fat. Still, its weakness is the inability to differentiate visceral fat from subcutaneous fat. In this study, we introduced epicardial fat thickness as a surrogate measure of visceral fat for the first

time to evaluate the association between visceral fat and bone mass. Epicardial fat is widely used in studies of diseases related to metabolic syndrome and atherosclerosis and it is known to have the same embryologic origin as intra-abdominal visceral fat. Epicardial fat thickness measured by transthoracic echocardiography has been highly associated with abdominal visceral fat quantity measured by MRI.[27] According to our study results, visceral fat estimated from epicardial fat and total FM are positively associated with BMC. The reason for the positive association between BMC and abdominal visceral fat was not evaluated in this study. The systemic effects of visceral fat such as hyperinsulinemia due to insulin resistance and altered sex hormone metabolism might be important factors and should be evaluated in future studies.[35,37]

BMD has been widely used as a surrogate marker for the diagnosis of osteoporosis and osteopenia, but, in this study, we used BMC as a surrogate and dependable variable for bone mass. BMD measured with DXA reflects areal BMD rather than volumetric BMD, and it likely overestimates and underestimates BMD for subjects who are larger and smaller than average size people, respectively.[38] Bone area is a major

component for calculating BMD and it is highly correlated with body size and FM. These limitations remove the association between fat and bone mass, so, in this study, we used BMC to study the associations between bone mass and body composition parameters.

This study has several strengths. Principally, it is the first study to demonstrate an association between visceral fat estimated from epicardial fat and bone mass. Also, we used diverse methods for estimating abdominal fat and considered a wide range of probable covariates that influence BMC, which allowed us to achieve an accurate estimation of the association between abdominal visceral fat and BMC. However, this study has several limitations. This study was a cross-sectional design and all participants were Korean. Therefore, it is impossible to establish causal relationships or generalize the findings to other ethnicities. Further, echocardiographic epicardial fat thickness may not reflect the exact quantity of total epicardial fat because it is a linear measurement and varies at different locations around the myocardium. In the future, large longitudinal studies that measure volumetric visceral fat will reveal the relationship between abdominal visceral fat and bone.

In conclusion, this study showed that abdominal visceral fat estimated from epicardial fat thickness was positively associated with BMC. These findings suggest that visceral fat has a protective effect on bone mass, which supports the obesity paradox.

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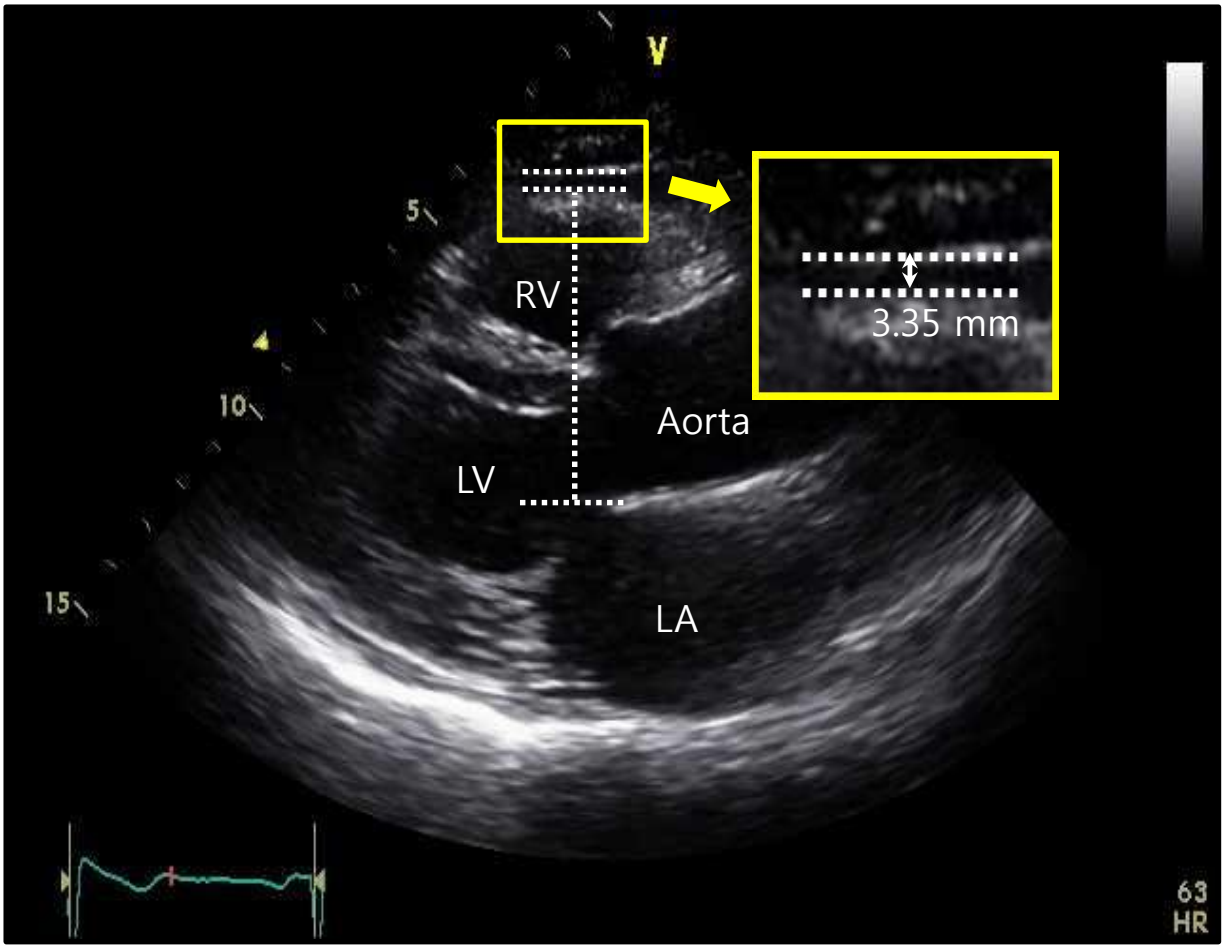


Figure 1. Measurement of epicardial fat thickness
Epicardial fat thickness was measured perpendicularly on the free wall of right ventricle from parasternal long axis view at end-systole.

Abbreviation : RV - right ventricle, LV - left ventricle, LA - left atrium

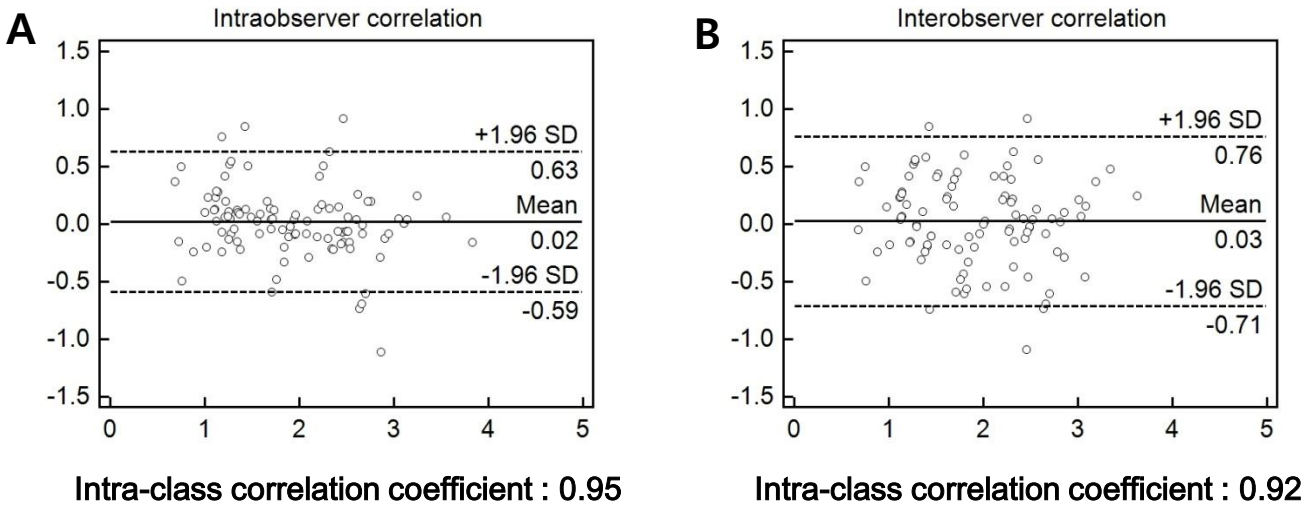


Figure 2.
The intra- and inter-observer agreement for epicardial fat thickness was expressed as Bland-Altman plot.

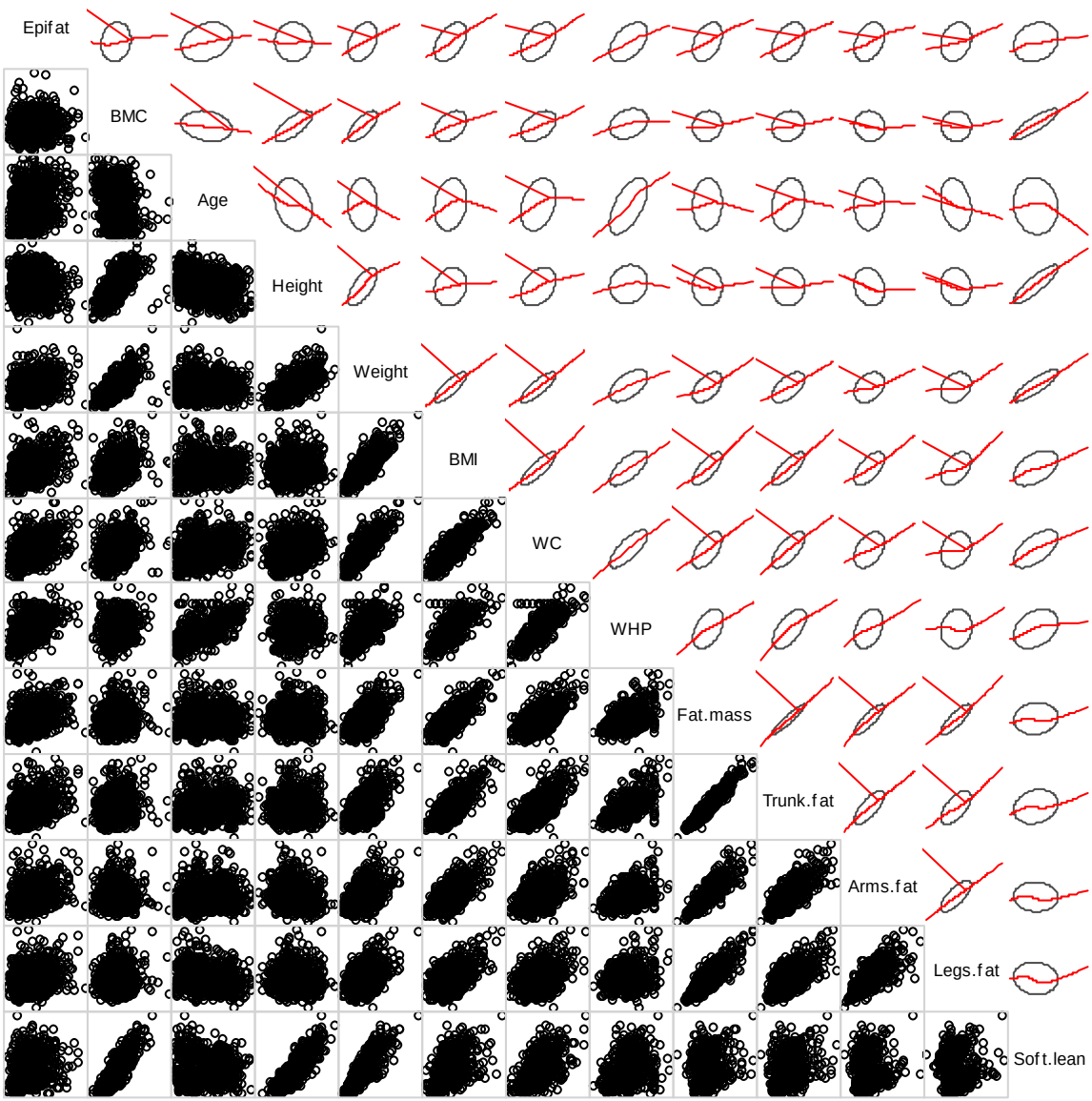


Figure 3. Correlogram of epicardial fat with anthopometric and body composition variables

Abbreviation)

Epifat – epicardial fat thickness, BMC – bone mineral content, BMI – body mass index, WC – waist circumference, WHR – waist to hip ratio

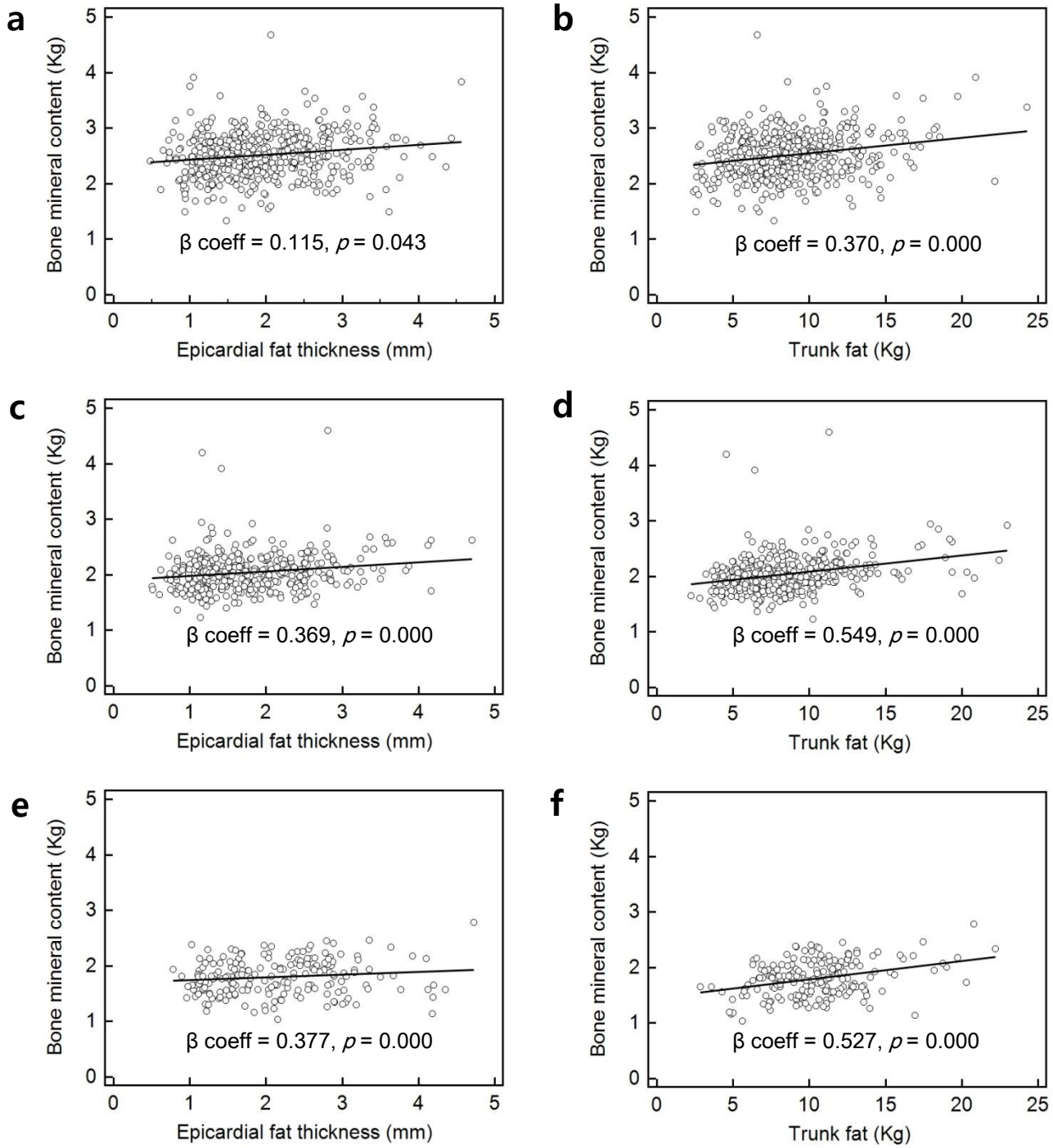
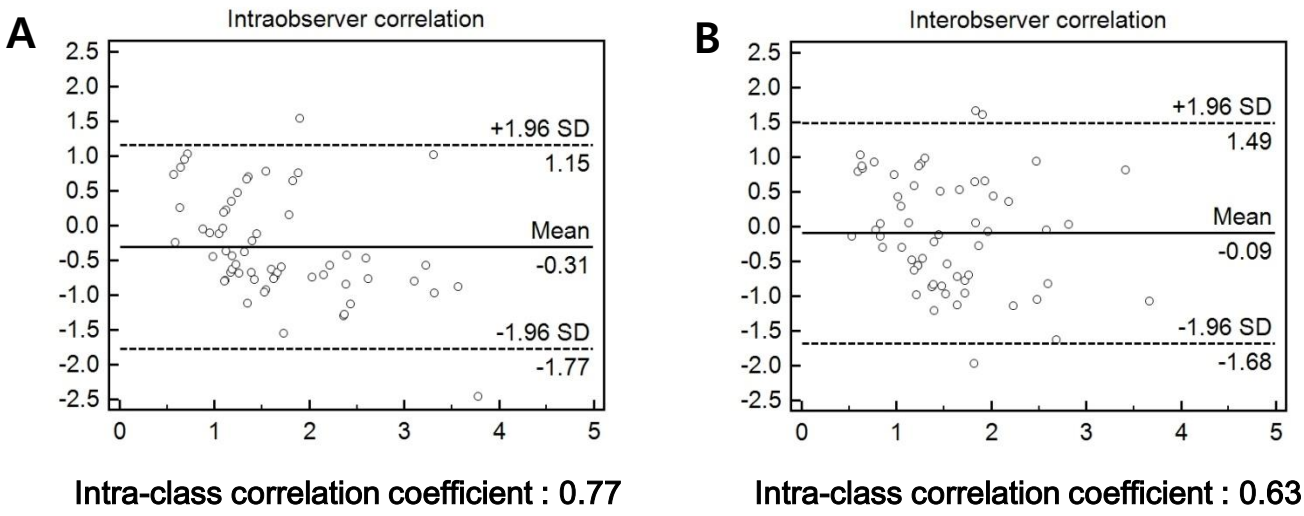


Figure 4.

Association between BMC and epicardial fat thickness or trunk fat.

a, b : Men; c, d : premenopausal women; e, f : postmenopausal women



Supplement figure 1.

The intra- and inter-observer agreement for epicardial fat thickness of excluded subjects due to poor echocardiographic image quality was expressed as Bland-Altman plot.

Table 1. Baseline characteristics of study population

Variables	Male (n=525)	Pre-menopausal women (n=460)	Post-menopausal women (n=213)	Total (n=1198)	P-value
Age (years)	44.2 ± 14.7	35.5 ± 8.4	56.2 ± 8.1	43.0 ± 13.	a,b,c
Epicardial fat thickness (mm)	1.93 ± 0.72	1.73 ± 0.72	2.17 ± 0.81	1.90 ± 0.75	a,b,c
BMC_whole body (kg)	2.51 ± 0.40	2.04 ± 0.33	1.80 ± 0.31	2.21 ± 0.46	a,b,c
BMD_whole (g/cm2)	1.17 ± 0.13	1.11 ± 0.19	1.03 ± 0.12	1.13 ± 0.16	a,b,c
BMD_spine (g/cm2)	0.98 ± 0.17	0.98 ± 0.13	0.88 ± 0.19	0.96 ± 0.16	b,c
BMD_pelvis (g/cm2)	1.15 ± 0.16	1.11 ± 0.13	1.06 ± 0.20	1.12 ± 0.16	a,b,c
Height (cm)	170.2 ± 8.5	158.2 ± 9.5	155.2 ± 5.4	162.9 ± 11	a,b,c
Weight (Kg)	71.6 ± 10.5	57.2 ± 9.2	58.4 ± 8.5	63.7 ± 11.9	a,b
BMI (Kg/m2)	24.5 ± 2.9	22.6 ± 3.2	24.2 ± 3.1	23.7 ± 3.2	a,c
Waist circumference (cm)	85.7 ± 7.9	76.1 ± 8.2	81.7 ± 8.4	81.3 ± 9.2	a,b,c
Waist to hip ratio	0.91 ± 0.21	0.84 ± 0.06	0.90 ± 0.06	0.88 ± 0.16	a,c
Fat mass (kg)	16.0 ± 5.4	17.9 ± 5.4	19.8 ± 5.1	17.4 ± 5.5	a,b,c
Percent fat mass (%)	22.5 ± 5.4	31.4 ± 6.1	34.4 ± 5.0	28.0 ± 7.5	a,b,c
Trunk fat mass (kg)	8.7 ± 3.3	8.5 ± 3.3	10.5 ± 3.2	9.0 ± 3.4	b,c
Percent trunk fat mass (%)	25.0 ± 6.6	30.6 ± 7.5	35.6 ± 6.3	29.0 ± 8.0	a,b,c
Head fat mass (kg)	1.2 ± 0.2	1.0 ± 1.1	1.0 ± 0.1	1.1 ± 0.7	a,b
Leg fat mass (kg)	4.4 ± 1.6	6.3 ± 1.7	5.8 ± 1.6	5.4 ± 1.9	a,b,c
Soft lean mass (kg)	52.4 ± 6.6	37.2 ± 4.7	36.0 ± 3.9	44.4 ± 9.6	a,b
Skeletal muscle mass (kg)	31.0 ± 4.3	21.3 ± 2.9	20.5 ± 2.4	25.9 ± 6.2	a,b
Hypertension (%)	17.0	2.6	27.7	13.4	a,b,c
Diabetes mellitus (%)	6.9	1.1	8.5	4.9	a,c
Hyperthyroidism (%)	0.6	2.6	0.9	1.4	a
Smokers (%)	67.4	12.8	5.2	35.7	a,b,c
Drinkers (%)	85.0	74.8	45.1	74.3	a,b,c
Regular exercise (%)	41.7	30	40.8	37.7	a,c

Data are expressed as means ± SD.

Post hoc analysis by independent t-test (mean difference between two groups):

a: men vs. premenopausal women; b: men vs. postmenopausal women; c: premenopausal vs. postmenopausal women.

Discrete variables were analyzed by the χ^2 test.

$P < 0.05$ was considered significant.

BMC: bone mineral content; BMD: bone mineral density; DXA: dual energy x-ray absorptiometry.

Table 2. Associations between epicardial fat thickness and body composition variables

	Male	Premenopausal women	Postmenopausal women	Total
Fat mass	0.368***	0.392***	0.484***	0.392***
Trunk fat mass	0.375***	0.388***	0.495***	0.423***
Arms fat mass	0.341***	0.336***	0.407***	0.340***
Legs fat mass	0.262***	0.301***	0.340***	0.220***
Head fat mass	0.241***	-0.037	0.274***	0.009
Height	0.008	0.069	-0.060	0.023
Weight	0.361***	0.393***	0.470***	0.338***
Waist	0.469***	0.393***	0.496***	0.444***
Hip	0.298***	0.317***	0.444***	0.326***
BMI	0.473***	0.437***	0.553***	0.519***
Waist to hip ratio	0.058	0.390***	0.611***	0.163***
Soft lean mass	0.136*	0.401***	0.418***	0.204***
Skeletal muscle mass	0.126*	0.400***	0.405***	0.197***

Data presented are Pearson correlation coefficients.

*P<0.05; **P<0.01; ***P<0.001

BMI: body mass index.

Table 3. Comparisons of the least squares means of bone mineral content (BMC) and bone mineral density (BMD) according to epicardial fat thickness tertiles adjusted for age and height

	Epicardial fat thickness			*p* for trend	P-value
	1st tertile	2nd tertile	3rd tertile		
Men					
BMC_whole (kg)	2.42 ± 0.03	2.51 ± 0.03	2.61 ± 0.03	0.000	a,b,c
BMD_whole (g/cm2)	1.16 ± 0.01	1.17 ± 0.01	1.19 ± 0.01	0.048	b
BMD_spine (g/cm2)	0.98 ± 0.01	0.98 ± 0.01	0.98 ± 0.01	0.978	-
BMD_pelvis (g/cm2)	1.12 ± 0.01	1.14 ± 0.01	1.18 ± 0.01	0.024	b,c
Premenopausal women					
BMC_whole (kg)	2.02 ± 0.02	2.01 ± 0.03	2.11 ± 0.03	0.029	b,c
BMD_whole (g/cm2)	1.11 ± 0.01	1.10 ± 0.01	1.13 ± 0.02	0.085	c
BMD_spine (g/cm2)	0.98 ± 0.01	0.97 ± 0.01	0.99 ± 0.01	0.397	-
BMD_pelvis (g/cm2)	1.09 ± 0.01	1.10 ± 0.01	1.14 ± 0.01	0.032	b,c
Postmenopausal women					
BMC_whole (kg)	1.72 ± 0.04	1.77 ± 0.03	1.87 ± 0.03	0.003	b,c
BMD_whole (g/cm2)	1.01 ± 0.02	1.02 ± 0.01	1.05 ± 0.01	0.063	b
BMD_spine (g/cm2)	0.84 ± 0.03	0.87 ± 0.02	0.91 ± 0.02	0.104	b
BMD_pelvis (g/cm2)	1.05 ± 0.03	1.03 ± 0.03	1.08 ± 0.02	0.014	a,b,c
Total					
BMC_whole (kg)	2.15 ± 0.02	2.20 ± 0.02	2.28 ± 0.02	0.000	a,b,c
BMD_whole (g/cm2)	1.11 ± 0.01	1.12 ± 0.01	1.15 ± 0.01	0.000	b,c
BMD_spine (g/cm2)	0.96 ± 0.01	0.95 ± 00	0.97 ± 0.01	0.000	-
BMD_pelvis (g/cm2)	1.09 ± 0.01	1.11 ± 0.01	1.15 ± 0.01	0.000	b,c

Data are expressed as means ± standard error of the mean.

Post hoc analysis using the least significant difference t-test (mean difference between two groups):

a: men vs. premenopausal women; b: men vs. postmenopausal women; c: premenopausal vs. postmenopausal women

Table 4. Gender-specific associations between bone mineral content and epicardial fat thickness and body composition variables by multiple linear regression analyses

	Men		Premenopausal women		Postmenopausal women		Total	
	β ± SE	P-value	β ± SE	P-value	β ± SE	P-value	β ± SE	P-value
Model 1								
Epicardial fat thickness	0.115 ± 0.021	0.000	0.069 ± 0.021	0.001	0.080 ± 0.023	0.001	0.083 ± 0.013	0.000
Waist to hip ratio	3.178 ± 0.465	0.000	1.027 ± 0.313	0.001	1.964 ± 0.528	0.000	2.033 ± 0.248	0.000
Trunk fat mass	0.020 ± 0.005	0.000	0.024 ± 0.004	0.000	0.032 ± 0.006	0.000	0.017 ± 0.003	0.000
Total fat mass	0.013 ± 0.003	0.000	0.015 ± 0.003	0.000	0.022 ± 0.004	0.000	0.009 ± 0.002	0.000
Soft lean mass	0.044 ± 0.003	0.000	0.046 ± 0.004	0.000	0.047 ± 0.008	0.000	0.040 ± 0.002	0.000
Model 2								
Epicardial fat thickness	0.119 ± 0.023	0.000	0.069 ± 0.023	0.003	0.076 ± 0.024	0.002	0.086 ± 0.014	0.000
Waist to hip ratio	3.843 ± 0.530	0.000	2.228 ± 0.381	0.000	1.939 ± 0.605	0.002	2.799 ± 0.283	0.000
Trunk fat mass	0.022 ± 0.005	0.000	0.023 ± 0.005	0.000	0.031 ± 0.006	0.000	0.019 ± 0.003	0.000
Total fat mass	0.015 ± 0.003	0.000	0.015 ± 0.003	0.000	0.021 ± 0.004	0.000	0.011 ± 0.002	0.000
Soft lean mass	0.046 ± 0.004	0.000	0.045 ± 0.004	0.000	0.047 ± 0.009	0.000	0.041 ± 0.002	0.000

SE: standard errors

Model 1: Covariates included in the regression model were age and height.

Model 2: Model 1 + additional adjustments for hypertension, diabetes, hyperthyroid disease, smoking habits, alcohol consumption, and regular exercise.

Table 5. Multivariable adjusted associations between bone mineral content and body composition variables using a linear mixed model

	Men		Premenopausal women		Postmenopausal women		Total	
	β ± SE	P-value	β ± SE	P-value	β ± SE	P-value	β ± SE	P-*value*
Epicardial fat thickness	0.107 ± 0.021	0.000	0.076 ± 0.022	0.001	0.058 ± 0.020	0.004	0.070 ± 0.013	0.000
Waist to hip ratio	3.760 ± 0.514	0.000	1.772 ± 0.473	0.000	2.200 ± 0.514	0.000	2.724 ± 0.293	0.000
Trunk fat mass	0.030 ± 0.005	0.000	0.027 ± 0.005	0.000	0.030 ± 0.005	0.000	0.021 ± 0.003	0.000
Total fat mass	0.020 ± 0.003	0.000	0.017 ± 0.003	0.000	0.020 ± 0.003	0.000	0.012 ± 0.002	0.000
Soft lean mass	0.045 ± 0.004	0.000	0.051 ± 0.005	0.000	0.049 ± 0.008	0.000	0.043 ± 0.003	0.000

SE: standard errors

The fixed effects (age, height, hypertension, diabetes, hyperthyroid disease, smoking habits, alcohol consumption, and regular exercise) and the random effect (family unit) were adjusted.

Supplemental Table 1. Baseline characteristics of the study population according to echocardiographic image quality

Variables	Good image (n=1198)	Poor image (n=209)	P-value
Age (years)	43.0 ± 13.7	38.6 ± 13.7	0.000
Men	43.8	47.8	0.022
Women			
Premenopausal	38.4	42.1	
Postmenopausal	17.8	10.0	
Epicardial fat thickness (mm)	1.90 ± 0.75	1.46 ± 0.67	0.000
BMC_whole body (kg)	2.21 ± 0.46	2.24 ± 0.46	0.161
Height (cm)	162.9 ± 10.7	164.4 ± 8.7	0.052
Weight (Kg)	63.7 ± 11.9	61.9 ± 12.3	0.039
BMI (Kg/m2)	23.7 ± 3.2	22.9 ± 3.5	0.011
Waist circumference (cm)	81.3 ± 9.2	78.4 ± 9.8	0.000
Waist to hip ratio	0.88 ± 0.16	0.85 ± 0.06	0.039
Fat mass (kg)	17.4 ± 5.5	15.5 ± 5.6	0.000
Trunk fat mass (kg)	9.0 ± 3.4	7.7 ± 3.4	0.000
Head fat mass (kg)	1.1 ± 0.7	1.0 ± 0.2	0.436
Soft lean mass (kg)	44.4 ± 9.6	44.5 ± 10.2	0.940
Skeletal muscle mass (kg)	25.9 ± 6.2	26.1 ± 6.6	0.853
Hypertension (%)	13.4	7.2	0.035
Diabetes mellitus (%)	4.9	4.3	0.545
Hyperthyroidism (%)	1.4	2.4	0.310
Smokers (%)	35.7	36.1	0.901
Drinkers (%)	74.3	77.4	0.387
Regular exercise (%)	37.7	33.2	0.696

Data are expressed as means ± SD.

Discrete variables were analyzed by the χ^2 test.

BMC: bone mineral content; BMD: bone mineral density; DXA: dual energy x-ray absorptiometry.

요약(국문초록)

심외막지방 측정을 통한 복부 내장 지방과 골무기질량의 연관성 분석

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복부내장지방이 심혈관계 및 대사성질환에 부정적인 영향을 주는 것으로 잘 알려져 있지만, 복부내장지방과 골다공증과의 관계는 아직 정립되어 있지 않다. 이번 연구에서는 경흉부심초음파를 이용해 측정한 심외막지방(epicardial fat)과 이중에너지 방사선흡수법(dual energy x-ray absorptiometry, DXA)을 통해 측정한 골무기질량(bone mineral content, BMC)의 연관성 분석을 통해 복부지방과 골다공증간의 관계를 밝혀보고자 하였다. 연구대상은 총 1198명 (남자 525명, 폐경전여성 460명, 폐경후 여성 213명)으로 한국형 쌍둥이 코호트연구(The Healthy Twin study)

에서 선정되었다. 심외막지방은 경흉부심초음파의 흉골연 장축단면도 (parasternal long axis view)에서 수축말기의 우심실 심근과 장측 심낭막 (visceral pericardium) 사이의 지방의 두께로 측정되었다. 전체 지방량, 부위별 지방량 및 제지방체중(lean body mass) 및 골무기질량은 DXA 방법으로 측정되었다. 연령 및 키를 보정한 다중선형회귀분석에서 복부내장 지방의 대체 측정치인 심외막지방의 두께는 남자, 여자 모두에서 골무기질량과 양의 상관관계를 보였다. 또한 과거질병력과 흡연력, 음주력, 규칙적인 운동상태 등을 추가 보정한 모델에서도 심외막지방과 골무기질량의 관계는 양의 상관관계로 나타났다. 이와 같은 연관성은 다른 방법 (waist circumference, Waist to hip ratio, trunk fat from DXA) 으로 측정된 복부지방지표와 골무기질량간의 연관성 분석에서 그대로 나타났다. 이러한 결과는 복부내장지방이 심혈관 질환 및 대상성 질환에 부정적인 영향을 주는 것에 비해, 골무기질량에는 긍정적인 영향을 미칠 가능성을 보여준다.

주요어 : 복부내장지방, 골무기질량, 심외막지방

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